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Abstract: The reaction of a rhodanine derivative (= (Z)-5-benzylidene-3-phenyl-2-thioxo-1,3-thiazolidin-4-one; 1) with (S)-2-methyl-oxirane (2) in the presence of SiO2 in dry CH2Cl2 for 10 days led to two diastereoisomeric spirocyclic 1,3-oxathiolanes 3 and 4 with the Me group at C(2) (Scheme 2). The analogous reaction of 1 with (R)-2-phenyloxirane (5) afforded also two diastereoisomeric spirocyclic 1,3-oxathiolanes 6 and 7 bearing the Ph group at C(3) (Scheme 3). The structures of 3, 4, 6, and 7 were confirmed by X-ray crystallography (Figs. 1 and 2). These results show that oxiranes react selectively with the thiocarbonyl group (C=S) in 1. Furthermore, the nucleophilic attack of the thiocarbonyl S-atom at the SiO2-activated oxirane ring proceeds with high regio- and stereoselectivity via an SN2-type mechanism.

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Regio- and Stereoselective Reactions of a Rhodanine Derivative with Optically Active 2-Methyl- and 2-Phenyloxirane

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Abstract The reaction of a rhodanine derivative (= 5-benzylidene-3-phenyl-2-thioxo-1,3-thiazolidin-4-one; **1**) with (*S*)-2-methyloxirane (**2**) in the presence of SiO_2 in dry CH_2Cl_2 for 10 d led to two diastereoisomeric spirocyclic 1,3-oxathiolanes **3** and **4** with the Me group at C(2) (Scheme 2). The analogous reaction of **1** with (*R*)-2-phenyloxirane (**5**) afforded also two diastereoisomeric spirocyclic 1,3-oxathiolanes **6** and **7** bearing the Ph group at C(3) (Scheme 3). The structures of **3**, **4**, **6**, and **7** were confirmed by X-ray crystallography (Figs. 1 and 2). These results show that oxiranes react selectively with the thiocarbonyl group (C=S) in **1**. Furthermore, the nucleophilic attack of the thiocarbonyl S-atom at the SiO_2-activated oxirane ring proceeds with high regio- and stereoselectivity *via* an S_N2-type mechanism.

1. Introduction

The reaction of thiocarbonyl compounds with oxiranes in the presence of a *Lewis* acid to give 1,3-oxathiolanes has been investigated thoroughly in recent years.[1–7] All results reported indicate that the reactions proceed with high regio- and

Keywords: rhodanine; oxiranes; 1,3-oxathiolanes; thiocarbonyl group; SiO_2; S_N2-type reaction.

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stereoselectivity *via* an S_N2-type mechanism. In the case of alkyl-substituted oxiranes, the thiocarbonyl S-atom attacks preferably at C(3) leading to the 5-substituted 1,3-oxathiolanes with retention of the configuration. On the other hand, the nucleophilic attack occurs mainly at C(2) of phenyloxirane to yield the 4-phenyl-substituted products *via* inversion of the configuration (Scheme 1).

Scheme 1

With the aim of establishing the scope and limitation of the formation of 1,3-oxathiolanes, the reactions of a rhodanine derivative, *i.e.* 5-benzylidene-3-phenyl-2-thioxo-1,3-thiazolidin-4-one (**1**) with optically active oxiranes were carried out. In the present paper, the results with (*S*)-2-methyloxirane (**2**) and (*R*)-2-phenyloxirane (**5**) are described.

2. Results

2.1. Reaction of the rhodanine derivative 1 with (*S*)-2-methyloxirane (2).

The reaction of **1** with **2** in a molar ratio of 1:4 was carried out in dry CH_2Cl_2 at room temperature under an N_2 atmosphere in the presence of SiO_2.[‡] After stirring for 10 d, filtration and the usual workup by means of column chromatography (CC) and preparative TLC (PLC) gave two diastereoisomeric spirocyclic 1,3-oxathiolanes **3** and **4** in 23 and 19% yield, respectively. The starting material **1** was recovered in 52% yield (Scheme 2). The enantiomeric excess (ee) of the products was determined by analytical HPLC (*(*S,S*)-Whelk-O 1*, hexane/AcOEt 3:1).

[‡] The analogous reaction with racemic 2-methyloxirane leading to racemic products of type **3** and **4** was also carried out.

Scheme 2

The structures of **3** and **4** were assigned on the basis of the elemental analyses, MS, IR, ^{1}H- and ^{13}C-NMR, 1D-NOESY, HSQC, HSQC-TOCSY, and HMBC spectra, which clearly indicated the relative configurations of the products. For example, on irradiation of H–C(2) at 4.50 ppm, the 1D-NOESY spectrum of **4** showed one NOE-signal for two *ortho* H-atoms of the PhN residue at 7.40–7.38 ppm, whereas this signal was missing in the analogous experiment with **3**. Finally, the structures were established by X-ray crystallography (Fig. 1).

Fig. 1

The crystals of **3** and **4** were enantiomerically pure and the absolute configurations of the molecules were determined independently by the diffraction experiments. Therefore, **3** has the (2*S*,5*R*)-configuration, whereas **4** is the (2*S*,5*S*)-diastereoisomer. In the case of **3**, the oxathiolane ring has an envelope conformation with C(3) as the envelope flap. The other five-membered ring shows a half-chair conformation twisted on S(6)–C(5), although the puckering is quite shallow and distorted towards an envelope. Both five-membered rings of **4** have a half-chair conformation twisted on C(2)–C(3) and S(6)–C(5), respectively.

The formation of **3** and **4** proceeded with retention of the configuration at C(2) of the oxirane **2** because the nucleophilic attack of the thiocarbonyl S-atom took place at C(3), leading to the intermediate **A**. Ring closure *via* nucleophilic addition of the O-atom at the thiocarbonylium group from the *si*- or *re*-side leads to **3** and **4**, respectively.

2.2. Reaction of the rhodanine derivative 1 with (*R*)-2-phenyloxirane (5).

The analogous reaction of **1** with **5** (molar ratio 1:2, dry CH_2Cl_2, room temperature, 10 d, N_2 atmosphere) in the presence of SiO_2 gave two diastereoisomeric spiroheterocycles **6** and **7** in 37 and 8% yield, respectively. In addition, **1** was recovered in 51% yield (Scheme 3). A likely intermediate is **B**. The determination of the ee-values by means of HPLC showed that **6** was formed *via* inversion of the configuration at C(2) of **5**. The formation of **7** proceeded with lower stereoselectivity and partial racemization (9%) was observed.[§] The structures of **6** and **7** were assigned on the basis of their elemental analyses and spectroscopic data, particularly 2D-NOESY, HSQC, HSQC-TOCSY, and HMBC spectra, and they were confirmed by X-ray crystallography (Fig. 2).

Scheme 3

The examination of a *Dreiding*-model of **6** shows that the distances between the *ortho*-H atoms of Ph–C(3) and those of Ph–N are small, in agreement with the 2D-NOESY spectrum of **6**, which shows one cross-signal between the *ortho*-H atoms of Ph–N at 7.33–7.30 ppm and those of Ph–C(3) at 6.55 ppm. Therefore, the configuration of **6** should be 3*S*,5*S*. Similarly, the 2D-NOESY spectrum of **7** shows one relevant cross-signal between the *ortho*-H atoms of Ph–N at 7.49–7.45 ppm and H–C(3) at 4.20 ppm, which, on the assumption that the reaction proceeded again with inversion of the configuration of **5**, indicates the (3*S*,5*R*)-configuration of **7**.

Fig. 2

[§] The analogous reaction with racemic 2-phenyloxirane gave the corresponding racemic products.

The crystals of **6** are enantiomerically pure and the absolute configuration of the molecule has been determined independently by the diffraction experiment and found to have the (3*S*,5*S*)-configuration. There are two symmetry-independent molecules in the asymmetric unit. Both are of the same enantiomer and differ primarily in the orientations of the phenyl rings, particularly the Ph–C(3), which in molecule A is rotated by 70° with respect to its orientation in molecule B. The 1,3-thiazolidine ring in molecule A has a flattened envelope conformation with the spiro C(5)-atom, as the envelope flap, while in molecule B, this ring is planar. The other five-membered ring in each molecule has the envelope conformation with C(2) acting as the envelope flap.

Although the enantiomeric excess of **7** amounted to 91% according to the analytical HPLC and the isolated product was optically active, the crystal used for the crystal-structure determination was racemic since the space group is centrosymmetric. The oxathiolane ring has a half-chair conformation twisted on C(2)–C(3). The other five-membered ring has a distorted shallow envelope conformation with S(6) as the envelope flap. The distortion is towards a half-chair twisted on S(6)–C(5).

3. Discussion and Conclusion

The five-membered ring of the rhodanine derivative **1** has been shown to be planar and the bond lengths involving S(1) indicate significant delocalization of the lone-pair electrons of S(1) with the adjacent C(2)=S and C(5)=C(1′) systems.[9] Therefore, the nucleophilic attack of **1** at the *Lewis* acid-complexed oxiranes could occur, in principle, either at the thiocarbonyl group (C(2)=S) or at the C(5)=C(1′) double bond. A third possibility is the reaction with the carbonyl

group (C(4)=O). However, the results presented show that the reactions of **1** with **2** and **5** take place chemoselectively at the thiocarbonyl group (C(2)=S) to yield the spirocyclic 1,3-oxathiolanes with high regio- and stereoselectivity. The results show that the C=S group is the most reactive nucleophile in **1**. We assume that the reactions proceed *via* an S_N2-type mechanism, whereby the nucleophilic thiocarbonyl S-atom favorably attacks the C(3)-atom (O–C(3) cleavage) of the activated (*S*)-2-methyloxirane (**2**) leading to intermediate **A** with retention of the configuration (Scheme 2). On the other hand, the addition to (*R*)-2-phenyloxirane (**5**) occurs selectively at the C(2)-atom (O–C(2) cleavage) with inversion of the configuration leading to intermediate **B** (Scheme 3). The partial loss of the stereochemical integrity of the phenyloxirane moiety in the formation of **7** may be interpreted by a competing reaction in which the oxirane ring-opening occurs prior to the nucleophilic attack (S_N1-type).

4. Experimental

4.1. General

See ref.[10] Optical rotations: *Perkin-Elmer 241* polarimeter (*c* = 1 in THF). IR Spectra: KBr, cm^{-1}. ^1H- and ^{13}C-NMR Spectra: in $CDCl_3$. Enantiomeric excesses (ee) were determined by anal. HPLC on a *(*S,S*)-Whelk-O 1* column (hexane/AcOEt 3:1).

4.2. Reactions of 5-benzylidene-3-phenyl-2-thioxo-1,3-thiazolidin-4-one (1) with (*S*)-2-methyloxirane (2) and (*R*)-2-phenyloxirane (5).

General procedure. To a solution of **1** (*ca.* 1 mmol) and oxirane **2** or **5** (2–4 mmol) in dry CH_2Cl_2 (10–15 mL) under an N_2 atmosphere, 4.5 g of silica gel (SiO_2) were added at rt. After stirring the suspension for 10 d at rt, the mixture was filtered and

the residue was washed with ethyl acetate (AcOEt, 4×). Then, the combined filtrate was evaporated *i.v.* The products were separated by chromatography (SiO_2, hexane/AcOEt; CC, MPLC, or prep. TLC (PLC)).

4.2.1. Reaction of 1 with (*S*)-2-methyloxirane (2).

Reaction of **1** (446 mg, 1.5 mmol) with **2** (348 mg, 6 mmol) and 4.5 g of SiO_2 at rt, 10 d; CC and prep. TLC (hexane/AcOEt 20:1) yielded 120 mg (23%) of **3** and 103 mg (19%) of **4**, and 230 mg (52%) of the starting material (**1**) was recovered .

(2*S*,5*R*)-7-Benzylidene-2-methyl-9-phenyl-1-oxa-4,6-dithia-9-azaspiro[4.4]nonan-8-one (3). Colorless crystals. M.p. 161.4 – 162.5°. $[\alpha]_D^{24}$ = – 9.3 (>98% ee). IR: 3061*w*, 3043*w*, 3026*w*, 3012*w*, 2979*w*, 2925*w*, 2815*w*, 1703*s*, 1611*m*, 1594*w*, 1493*m*, 1447*w*, 1377*w*, 1356*s*, 1337*m*, 1222*m*, 1194*m*, 1171*w*, 1143*m*, 1131*m*, 1081*m*, 1020*s*, 986*s*, 926*m*, 897*w*, 870*w*, 806*w*, 758*m*, 733*m*, 697*m*, 687*m*. ^{1}H-NMR (300 MHz): 7.66 (*s*, PhC*H*); 7.52–7.30 (*m*, 10 arom. H); 4.41–4.30 (*m*, H–C(2)); 2.89 (*dd*, *J* = 10.4, 3.9, 1 H–C(3)); 2.15 (*t*-like, *J* ≈ 10.5, 1 H–C(3)); 1.34 (*d*, *J* = 6.0, Me). ^{13}C-NMR (75.5 MHz): 164.9 (*s*, C=O); 135.4, 134.7 (2*s*, 2 arom. C); 130.5, 129.8, 128.84, 128.77, 128.73 (5*d*, 10 arom. CH); 127.8 (*d*, Ph*C*H); 124.7 (*s*, C(7)); 109.9 (*s*, C(5)); 80.1 (*d*, C(2)); 40.8 (*t*, C(3)), 18.2 (*q*, Me). ESI-MS (MeOH+NaI): 733 (15, $[2M+Na]^+$), 378 (100, $[M+Na]^+$). Anal. calc. for $C_{19}H_{17}NO_2S_2$ (355.48): C 64.20, H 4.82, N 3.94, S 18.04; found: C 64.27, H 4.90, N 3.93, S 17.97. Crystals of **3** suitable for an X-ray crystal-structure analysis were grown from Et_2O/hexane.

(2*S*,5*S*)-7-Benzylidene-2-methyl-9-phenyl-1-oxa-4,6-dithia-9-azaspiro[4.4]nonan-8-one (4). Colorless crystals. M.p. 155.0 – 156.6°. $[\alpha]_D^{24}$ = + 114.6 (>98% ee). IR: 3076*w*, 3055*w*, 3039*w*, 3023*w*, 2989*w*, 2970*w*, 2943*w*, 2928*w*, 2862*w*,

2853*w*, 1679*s*, 1609*m*, 1594*w*, 1493*m*, 1447*w*, 1436*w*, 1373*m*, 1360*s*, 1312*w*, 1289*w*, 1238*w*, 1219*w*, 1191*m*, 1178*w*, 1170*w*, 1135*m*, 1104*m*, 1074*w*, 1058*w*, 1014*s*, 982*s*, 931*s*, 806*w*, 761*s*, 732*s*, 694*s*. ^{1}H-NMR (500 MHz): 7.65 (*s*, PhC*H*); 7.50–7.41 (*m*, 7 arom. H); 7.40–7.38 (*m*, 2 arom. H); 7.35–7.32 (*m*, 1 arom. H); 4.51–4.47 (*m*, H–C(2)); 2.77 (*dd*, *J* = 10.6, 3.6, 1 H–C(3)); 2.65 (*dd*, *J* = 10.7, 5.7, 1 H–C(3)); 1.41 (*d*, *J* = 6.3, Me). ^{13}C-NMR (125.8 MHz): 164.4 (*s*, C=O); 135.3, 134.7 (2*s*, 2 arom. C); 130.7, 129.7, 129.1, 129.0, 128.73, 128.70 (6*d*, 10 arom. CH); 127.3 (*d*, Ph*C*H); 124.5 (*s*, C(7)); 110.6 (*s*, C(5)); 81.8 (*d*, C(2)); 41.0 (*t*, C(3)), 19.5 (*q*, Me). ESI-MS (MeOH+NaI): 733 (25, $[2M+Na]^+$), 378 (100, $[M+Na]^+$). Anal. calc. for $C_{19}H_{17}NO_2S_2$ (355.48): C 64.20, H 4.82, N 3.94, S 18.04; found: C 64.18, H 4.94, N 3.91, S 18.02. Crystals of **4** suitable for an X-ray crystal-structure analysis were grown from Et_2O/hexane.

4.2.2. Reaction of 1 with (*R*)-2-phenyloxirane (5).

Reaction of **1** (297 mg, 1 mmol) with **5** (240 mg, 2 mmol) and 4.5 g of SiO_2 at rt, 10 d; CC and MPLC (hexane/AcOEt 15:1) yielded 153 mg (37%) of **6** and 32 mg (8%) of **7**, and 151 mg (51%) of the starting material (**1**) was recovered (Scheme 3).

(3*S*,5*S*)-7-Benzylidene-3,9-diphenyl-1-oxa-4,6-dithia-9-azaspiro[4.4]nonan-8-one (6). Colorless crystals. M.p. 218.6 – 222.9° (partially decomposed). $[\alpha]_D^{24}$ = – 12.3 (98% ee). IR: 3058*w*, 3032*w*, 2970*w*, 2926*w*, 2871*w*, 1690*vs*, 1608*m*, 1594*w*, 1493*s*, 1453*w*, 1446*m*, 1358*vs*, 1347*vs*, 1291*w*, 1280*w*, 1243*m*, 1234*s*, 1201*s*, 1185*w*, 1171*m*, 1155*m*, 1080*w*, 1072*w*, 1053*vs*, 1041*vs*, 1002*w*, 967*m*, 940*w*, 914*w*, 898*m*, 864*w*, 797*m*, 774*w*, 762*m*, 754*m*, 735*m*, 728*m*, 702*s*, 693*s*, 687*s*. ^{1}H-NMR (600 MHz): 7.62 (*s*, PhC*H*); 7.45 (*d*, *J* = 7.5, 2 arom. H); 7.42–7.27 (*m*, 8 arom. H); 7.02 (*t*, *J* = 7.4, 1 arom. H); 6.92 (*t*-like, *J* ≈ 7.7, 2 arom. H);

6.55 (*d*, *J* = 7.4, 2 arom. H); 4.72 (*dd*, *J* = 5.8, 2.5, H–C(3)); 4.37 (*dd*, *J* = 9.8, 5.8, 1 H–C(2)); 4.17 (*dd*, *J* = 9.8, 2.6, 1 H–C(2)). ^{13}C-NMR (150.9 MHz): 165.7 (*s*, C=O); 139.3, 135.3, 134.7 (3*s*, 3 arom. C); 131.6, 129.9, 129.1, 128.9, 128.8, 128.4 (6*d*, 12 arom. CH); 127.9 (*d*, Ph*C*H); 127.5, 127.0 (2*d*, 3 arom. CH); 124.0 (*s*, C(7)); 112.9 (*s*, C(5)); 75.9 (*t*, C(2)); 54.3 (*d*, C(3)). ESI-MS (MeOH/CH_2Cl_2+NaI): 859 (8), 858 (15), 857 (26, $[2M+Na]^+$), 442 (14), 441 (30), 440 (100, $[M+Na]^+$). CI-MS (NH_3): 418 (12, $[M+H]^+$), 301 (12), 300 (21), 299 (100), 282 (17), 256 (7). Anal. calc. for $C_{24}H_{19}NO_2S_2$ (417.55): C 69.04, H 4.59, N 3.35, S 15.36; found: C 68.86, H 4.50, N 3.29, S 15.20. Crystals of **6** suitable for an X-ray crystal-structure analysis were grown from CH_2Cl_2.

(3*S*,5*R*)-7-Benzylidene-3,9-diphenyl-1-oxa-4,6-dithia-9-azaspiro[4.4]nonan-8-one (7). Colorless crystals. M.p. 150.3 – 153.7°. $[\alpha]_D^{24}$ = – 152.8 (91% ee). IR: 3057*w*, 3028*w*, 2926*w*, 2863*w*, 1697*vs*, 1611*m*, 1595*w*, 1492*s*, 1453*m*, 1447*m*, 1345*vs*, 1227*m*, 1196*s*, 1150*m*, 1078*m*, 1052*vs*, 1040*s*, 944*w*, 900*w*, 866*w*, 801*w*, 761*s*, 736*w*, 692*vs*. ^{1}H-NMR (500 MHz, at 240K): 7.73 (*s*, PhC*H*); 7.58–7.31 (*m*, 15 arom. H); 4.49 (*dd*, *J* = 9.7, 5.4, 1 H–C(2)); 4.20 (*dd*, *J* = 10.7, 5.4, H–C(3)); 4.03 (*t*-like, *J* ≈ 10.2, 1 H–C(2)). ^{13}C-NMR (125.8 MHz, at 240K): 165.3 (*s*, C=O); 135.0, 134.21, 133.19 (3*s*, 3 arom. C); 130.1, 129.9, 129.2, 129.13, 129.05, 128.85, 128.83, 128.7, 128.33 (9*d*, 15 arom. CH); 128.26 (*d*, Ph*C*H); 123.8 (*s*, C(7)); 111.4 (*s*, C(5)); 76.5 (*t*, C(2)); 55.2 (*d*, C(3)). ESI-MS (MeOH+NaI): 859 (6), 858 (15), 857 (25, $[2M+Na]^+$), 442 (15), 441 (30), 440 (100, $[M+Na]^+$). Anal. calc. for $C_{24}H_{19}NO_2S_2$ (417.55): C 69.04, H 4.59, N 3.35, S 15.36; found: C 69.21, H 4.76, N 3.31, S 15.21. Crystals of *rac*-**7** suitable for an X-ray crystal-structure analysis were grown from Et_2O/hexane.

4.3. X-Ray Crystal-Structure Determination of 3, 4, 6, and 7.

See Figs. 1 and 2.[11] All measurements were made at 160K on a *Nonius KappaCCD* diffractometer[12] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream* 700 cooler. Data reductions were performed with *HKL Denzo* and *Scalepack*.[13] The intensities were corrected for *Lorentz* and polarization effects, and, in the cases of **3**, **4**, and **7**, an absorption correction based on the multi-scan method[14] was applied. Equivalent reflections, other than *Friedel* pairs, were merged. The structures were solved by direct methods using SIR92,[15] which revealed the positions of all non-H-atoms. In the case of **6**, there were two symmetry-independent molecules in the asymmetric unit. The atomic coordinates of the two molecules were tested carefully for a relationship from a higher symmetry space group using the program PLATON,[16] but none could be found, although there is a pseudo-inversion centre relating 89% of the atoms. The non-H-atoms were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to $1.2U_{eq}$ of its parent atom ($1.5U_{eq}$ for methyl groups). Refinements of the structures were carried out on F^2 using full-matrix least-squares procedures, which minimised the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied in the cases of **3**, **6**, and **7**. In **4** and **6**, one and two reflections, respectively, whose intensities were considered to be extreme outliers, were omitted from the final refinement. Refinements of the absolute structure parameter[17] yielded values of – 0.04(5), – 0.04(7), and 0.00(4) for **3**, **4**, and **6**, respectively, which confidently confirm that the refined coordinates represent the true enantiomorph in each case. For **7**, the largest peak of residual electron density lies within the oxathiolane ring in the vicinity of O(1) and C(2), but is inappropriately positioned to be correlated with disorder. Neutral atom scattering factors for non-H-atoms were taken from[18a] and the scattering factors for H-atoms

were taken from.[19] Anomalous dispersion effects were included in F_c;[20] the values for f' and f'' were those of.[18b] The values of the mass attenuation coefficients are those of.[18c] All calculations were performed using the *SHELXL97*[21] program.

Crystal data for **3**: $C_{19}H_{17}NO_2S_2$, M = 355.48, colorless, prism, crystal dimensions 0.12 × 0.15 × 0.28 mm, orthorhombic, space group $P2_12_12_1$, Z = 4, reflections for cell determination 57014, 2θ range for cell determination 4 – 60°, a = 5.6543(1) Å, b = 12.0695(2) Å, c = 25.3032(4) Å, V = 1726.81(5) Å^3, D_X = 1.367 g·cm^{-3}, μ(MoK_α) = 0.319 mm^{-1}, transmission factors (min; max) 0.876; 0.966, $2\theta_{(max)}$ = 60°, total reflections measured 30374, symmetry independent reflections 5021, reflections with $I > 2\sigma(I)$ 4222, parameters refined 219, R [on F; $I > 2\sigma(I)$ reflections] = 0.0338, $wR(F^2)$[all reflections] = 0.0777 ($w = [\sigma^2(F_o^2) + (0.0323P)^2 + 0.3459P]^{-1}$, where $P = (F_o^2+2F_c^2)/3$), goodness of fit 1.032, secondary extinction coefficient 0.005(1), final Δ_{max}/σ 0.001, $\Delta\rho$ (max; min) = 0.34; – 0.25 e Å^{-3}.

Crystal data for **4**: $C_{19}H_{17}NO_2S_2$, M = 355.48, colorless, tablet, crystal dimensions 0.07 × 0.15 × 0.25 mm, orthorhombic, space group $P2_12_12_1$, Z = 4, reflections for cell determination 35017, 2θ range for cell determination 4 – 60°, a = 5.5855(1) Å, b = 7.8820(1) Å, c = 39.0360(6) Å, V = 1718.56(5) Å^3, D_X = 1.374 g·cm^{-3}, μ(MoK_α) = 0.321 mm^{-1}, transmission factors (min; max) 0.863; 0.979, $2\theta_{(max)}$ = 60°, total reflections measured 25282, symmetry independent reflections 4973, reflections with $I > 2\sigma(I)$ 3564, parameters refined 218, R [on F; $I > 2\sigma(I)$ reflections] = 0.0425, $wR(F^2)$[all reflections] = 0.0871 ($w = [\sigma^2(F_o^2) + (0.0318P)^2 + 0.2116P]^{-1}$, where $P = (F_o^2+2F_c^2)/3$), goodness of fit 1.040, final Δ_{max}/σ 0.001, $\Delta\rho$ (max; min) = 0.41; – 0.33 e Å^{-3}.

Crystal data for **6**: $C_{24}H_{19}NO_2S_2$, M = 417.55, colorless, tablet, crystal dimensions 0.12 × 0.15 × 0.18 mm, monoclinic, space group $P2_1$, Z = 4, reflections for cell determination 4714, 2θ range for cell determination 4 – 55°, a = 8.5993(1) Å, b = 14.2768(2) Å, c = 16.5468(2) Å, β = 103.5458(6)°, V = 1974.95(4) Å^3, D_X = 1.404 g·cm^{-3}, μ(MoK_α) = 0.291 mm^{-1}, $2\theta_{(max)}$ = 55°, total reflections measured 45245, symmetry independent reflections 9001, reflections with $I > 2\sigma(I)$ 7665, parameters refined 524; restraints 1, R [on F; $I > 2\sigma(I)$ reflections] = 0.0402, wR (F^2)[all reflections] = 0.0970 ($w = [\sigma^2(F_o^2) + (0.0421P)^2 + 0.2619P]^{-1}$, where $P = (F_o^2+2F_c^2)/3$), goodness of fit 1.053, secondary extinction coefficient 0.0052(9), final Δ_{max}/σ 0.001, $\Delta\rho$ (max; min) = 0.38; – 0.41 e Å^{-3}. The structure of *rac*-**6** was also determined and the data have been deposited.[11]

Crystal data for *rac*-**7**: $C_{24}H_{19}NO_2S_2$, M = 417.55, colorless, prism, crystal dimensions 0.10 × 0.18 × 0.18 mm, triclinic, space group $P\bar{1}$, Z = 2, reflections for cell determination 29642, 2θ range for cell determination 4 – 60°, a = 8.5150(2) Å, b = 11.0168(2) Å, c = 12.1739(4) Å, α = 112.9576(9)°, β = 92.4883(9)°, γ = 95.597(2)°, V = 1042.40(5) Å^3, D_X = 1.330 g·cm^{-3}, μ(MoK_α) = 0.275 mm^{-1}, transmission factors (min; max) 0.859; 0.980, $2\theta_{(max)}$ = 60°, total reflections measured 28717, symmetry independent reflections 6086, reflections with $I > 2\sigma(I)$ 4405, parameters refined 263, R [on F; $I > 2\sigma(I)$ reflections] = 0.0568, wR (F^2)[all reflections] = 0.1580 ($w = [\sigma^2(F_o^2) + (0.0615P)^2 + 0.8250P]^{-1}$, where $P = (F_o^2+2F_c^2)/3$), goodness of fit 1.024, secondary extinction coefficient 0.015(4), final Δ_{max}/σ 0.001, $\Delta\rho$ (max; min) = 1.06; – 0.49 e Å^{-3}. Crystals of a second polymorph of *rac*-**7** were obtained from CH_2Cl_2. The structure of this polymorph was also determined and the data have been deposited.[11]

5. Acknowledgement

We thank the analytical services of our institute for NMR and mass spectra and elemental analyses, Mr. *B. Bürgi* for his assistance with the determination of the crystal structures and the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for financial support.

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11. CCDC-225511 – 225516 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax: +44-(0)1223-336033; e-mail: deposit@ccdc.cam.ac.uk).
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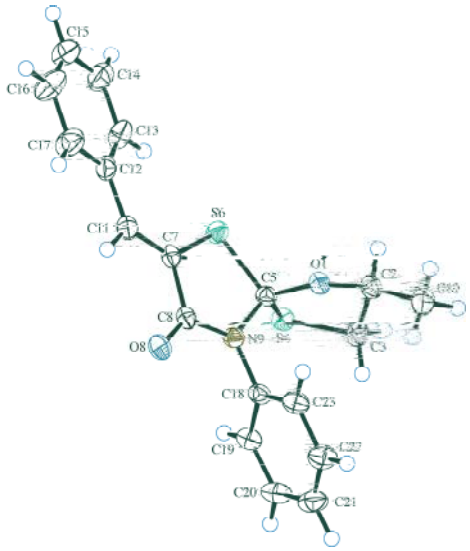
Captions:

Fig. 1. *ORTEP Plots*[8] of the molecular structures of a) **3** and b) **4** (displacement ellipsoids with 50% probability)

Fig. 2. *ORTEP Plots*[8] of the molecular structures of a) one of the two symmetry-independent molecules of **6** and b) of **7** (displacement ellipsoids with 50% probability)

Fig. 1

a)


C15
C14
C16
C13
C17
C12
C11
S6
C7
C5
O1
C2
C8
O8
N9
S4
C3
C18
C23
C19
C22
C20
C21

b)

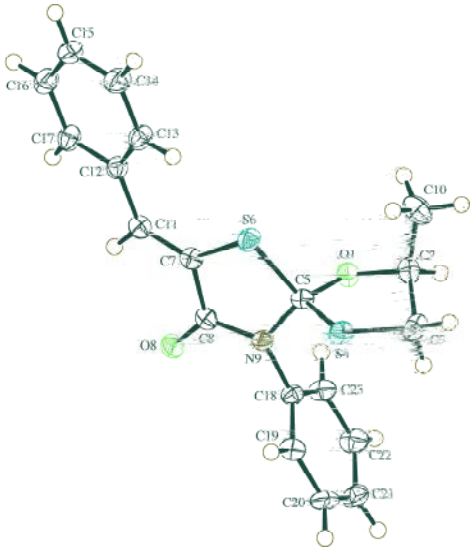
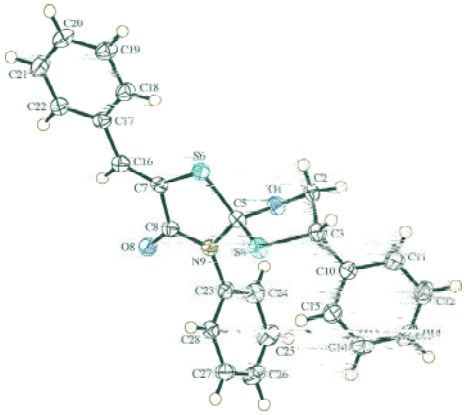
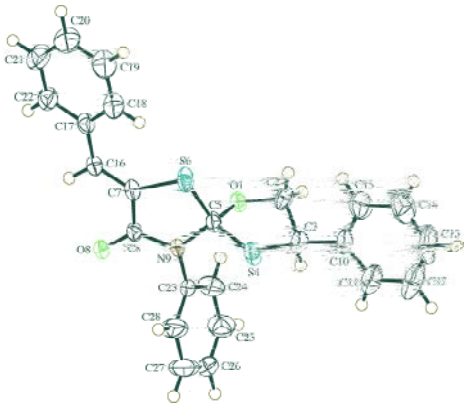

C15
C16
C14
C17
C13
C12
C11
C10
S6
C7
O1
C2
C5
O8
C8
N9
S4
C3
C18
C23
C19
C22
C20
C21

Fig. 2

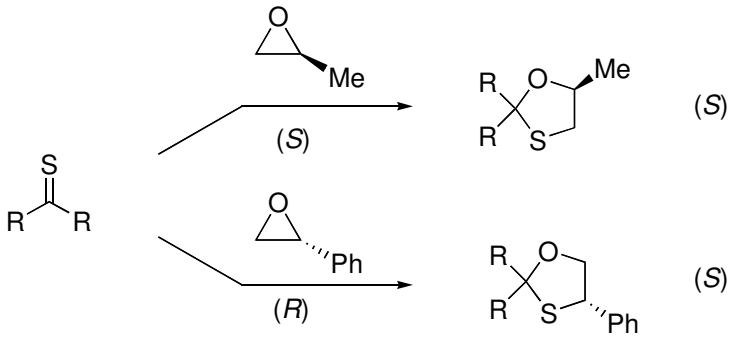
a)


C20
C19
C21
C18
C22
C17
C16
S6
C7
C5
O1
C2
C8
O8
N9
S4
C3
C10
C11
C23
C24
C15
C12
C28
C25
C27
C26

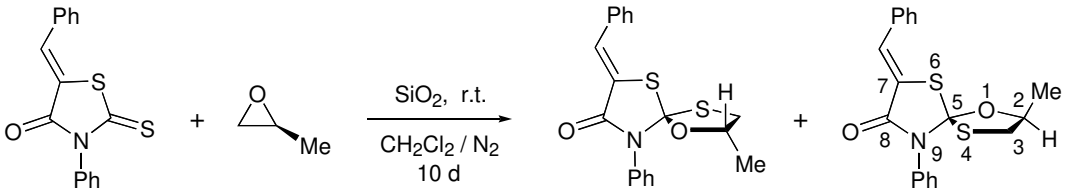
b)


C20
C21
C19
C22
C18
C17
C16
S6
C7
O1
C5
C2
C15
C14
C13
O8
C8
N9
S4
C3
C10
C11
C23
C24
C28
C25
C27
C26

Scheme 1

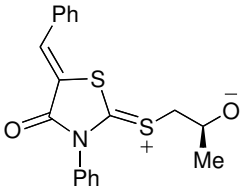


Scheme 2



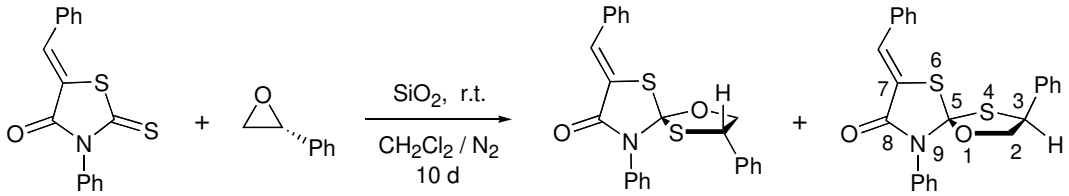
1 **2** **3** **4**

23% (>99% ee) 19% (>99% ee)



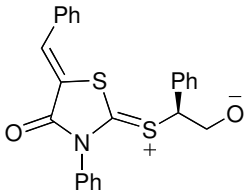
A

Scheme 3



1 **5** **6** **7**

37% (98% ee) 8% (91% ee)



B

Graphical Abstract

Regio- and Stereoselective Reactions of a Rhodanine Derivative with Optically Active 2-Methyl- and 2-Phenyl-oxiranes

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